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chain nodes :
2
ring nodes :
1 3 4 5 6 7 8
chain bonds :
1-2
ring bonds :
1-3 1-4 1-5 1-6 1-7 1-8 3-5 4-6 7-8
exact/norm bonds :
1-3 1-4 1-5 1-6 1-7 1-8 3-5 4-6 7-8
exact bonds :
1-2
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Match level :
1:Atom 2:CLASS 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom
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L1 STRUCTURE UPLOADED

=> d his

(FILE 'HOME' ENTERED AT 18:37:06 ON 19 NOV 2009)

FILE 'REGISTRY' ENTERED AT 18:37:14 ON 19 NOV 2009

L1 STRUCTURE UPLOADED

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=> d l1
L1 HAS NO ANSWERS
L1          STR
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Structure attributes must be viewed using STN Express query preparation.

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=> s l1
SAMPLE SEARCH INITIATED 18:37:39 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      38 TO ITERATE

100.0% PROCESSED      38 ITERATIONS      1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                       BATCH   **COMPLETE**
PROJECTED ITERATIONS:   391 TO    1129
PROJECTED ANSWERS:      1 TO      80

L2          1 SEA SSS SAM L1
```

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=> s l1 full
FULL SEARCH INITIATED 18:37:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      969 TO ITERATE

100.0% PROCESSED      969 ITERATIONS      6 ANSWERS
SEARCH TIME: 00.00.01

L3          6 SEA SSS FUL L1
```

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=> fil caplus
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                               ENTRY      SESSION
FULL ESTIMATED COST          185.88      186.10
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=> s l3

L4 8 L3

=> d 1-8 bib abs

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2008:1233615 CAPLUS

DN 151:349420

TI Oxidation of organosulfur compounds by hydrogen peroxide in the presence of niobium and vanadium peroxo complexes

AU Fam Vin', Tkhai; Tarakanova, A. V.; Kostyuchenko, O. V.; Tarasevich, B. N.; Kulikov, N. S.; Anisimov, A. V.

CS Faculty of Chemistry, Moscow State University, Moscow, Russia

SO Theoretical Foundations of Chemical Engineering (2008), 42(5), 636-642  
CODEN: TFCEAU; ISSN: 0040-5795

PB Pleiades Publishing, Ltd.

DT Journal

LA English

AB New niobium(V) peroxo complexes containing asparagine and Schiff base ligands were synthesized, and their structures were solved by IR, NMR, and mass spectrometric methods. They are catalytically active for the peroxidn. of Me Ph sulfide and benzothiophene to the corresponding sulfoxide and sulfones. Vanadium(V) peroxo complexes with the same ligands are less active in the oxidation of Me Ph sulfide than the niobium complexes.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2008:569319 CAPLUS

DN 150:486317

TI Synthesis and properties of potassium oxotriperoxovanadate(V) K3[VO(O-O)3]  
AU Titova, K. V.; Nikol'skaya, V. P.; Buyanov, V. V.; Pudova, O. B.;  
Karzhavina, G. P.; Oboznaya, Yu. G.

CS Institute for Problems of Chemical Physics, Russian Academy of Sciences,  
Chernogolovka, Russia

SO Russian Journal of Applied Chemistry (2008), 81(3), 392-394  
CODEN: RJACEO; ISSN: 1070-4272

PB Pleiades Publishing, Ltd.

DT Journal

LA English

AB The conditions of synthesis of potassium oxotriperoxovanadate(V) K3[VO(O-O)3] were developed, and the compound was isolated pure. Its physicochem. characteristics, including x-ray diffraction pattern, thermogravimetric data, and IR spectrum, are presented.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD

## ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2001:247735 CAPLUS  
 DN 135:66750  
 TI Gas-Phase Chemistry of Bare V+ Cation with Oxygen and Water at Room  
 Temperature: Formation and Hydration of Vanadium Oxide Cations  
 AU Koyanagi, Gregory K.; Bohme, Diethard K.; Kretzschmar, Ilona; Schroeder,  
 Detlef; Schwarz, Helmut  
 CS Department of Chemistry Centre for Research in Mass Spectrometry Centre  
 for Research in Earth and Space Science, York University, Toronto, ON, M3J  
 1P3, Can.  
 SO Journal of Physical Chemistry A (2001), 105(17), 4259-4271  
 CODEN: JPACAH; ISSN: 1089-5639  
 PB American Chemical Society  
 DT Journal  
 LA English  
 AB Mass spectrometric expts. at extremely low (<10<sup>-6</sup> mbar) and moderate (0.5  
 mbar) pressures are used to examine the reactions of atomic vanadium cation  
 with mol. oxygen and water. With O<sub>2</sub>, rapid O-atom abstraction gives rise  
 to the formation of VO<sup>+</sup> cation ( $k = 3 + 10^{-10}$  cm<sup>3</sup> mol.<sup>-1</sup> s<sup>-1</sup>).  
 Interestingly, despite a similar thermochem., the O-atom transfer from  
 water to bare V<sup>+</sup> is less efficient by more than an order of magnitude ( $k =$   
 $8 + 10^{-12}$  cm<sup>3</sup> mol.<sup>-1</sup> s<sup>-1</sup>). Subsequent assocns. of VO<sup>+</sup> with either  
 O<sub>2</sub> or H<sub>2</sub>O occur with very low efficiencies and involve termol.  
 stabilization mechanisms. The low probability of degenerate 16O/18O  
 exchange between VO<sup>+</sup> and water indicates the operation of a sizable  
 kinetic barrier. Ab initio calcns. using d. functional theory lend  
 further support to the interpretation of the exptl. data and provide the  
 first thermochem. information on VO<sup>+</sup> cations with  $n > 2$ , as well as some  
 hydrated species. In general, the dipolar water ligand is found to be  
 much more strongly bound to the cationic vanadium complexes than is  
 dioxygen.

OSC.G 42 THERE ARE 42 CAPLUS RECORDS THAT CITE THIS RECORD (42 CITINGS)  
 RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2001:3275 CAPLUS  
 DN 134:178239  
 TI Multinuclear NMR spectroscopic characterization of vanadium(V) alkylperoxo  
 complexes VO(OOtBu)<sub>k</sub>(OnBu)<sub>3-k</sub>, where  $k = 1, 2, 3$   
 AU Babushkin, D. E.; Talsi, E. P.  
 CS Borekov Institute of Catalysis, Novosibirsk, 630090, Russia  
 SO Reaction Kinetics and Catalysis Letters (2000), 71(1), 115-120  
 CODEN: RKCLAU; ISSN: 0304-4122  
 PB Akademiai Kiado  
 DT Journal  
 LA English  
 AB Using 51V, 17O, 13C and 1H NMR spectroscopy, vanadium(V) alkylperoxo  
 complexes VO(OOtBu)<sub>k</sub>(OnBu)<sub>3-k</sub>, where  $k = 1, 2$  and  $3$ , were characterized in  
 situ in the reaction of VO(OnBu)<sub>3</sub> with tBuOOH in CH<sub>2</sub>Cl<sub>2</sub>.

OSC.G 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)  
 RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 1985:533849 CAPLUS  
 DN 103:133849  
 OREF 103:21239a,21242a  
 TI High-field vanadium-51 and oxygen-17 nuclear magnetic resonance study of  
 peroxovanadates(V)

AU Harrison, Aidan T.; Howarth, Oliver W.  
CS Dep. Chem., University of Warwick, Coventry, CV4 7AL, UK  
SO Journal of the Chemical Society, Dalton Transactions: Inorganic Chemistry  
(1972-1999) (1985), (6), 1173-7  
CODEN: JCDTBI; ISSN: 0300-9246

DT Journal  
LA English

AB High-field 51V and 17O NMR spectra were determined for peroxyvanadates in aqueous

solution; 5 new species, including 4 which are dimeric, were identified. Mono- and diperoxyvanadates change from octahedral to tetrahedral coordination when their final proton is removed.

OSC.G 44 THERE ARE 44 CAPLUS RECORDS THAT CITE THIS RECORD (45 CITINGS)

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1980:51133 CAPLUS

DN 92:51133

OREF 92:8335a,8338a

TI Peroxo complexes of vanadium(V); a vanadium-51 nuclear magnetic resonance study

AU Howarth, Oliver W.; Hunt, John R.

CS Dep. Chem. Mol. Sci., University of Warwick, Coventry, CV4 7AL, UK

SO Journal of the Chemical Society, Dalton Transactions: Inorganic Chemistry  
(1972-1999) (1979), (9), 1388-91

CODEN: JCDTBI; ISSN: 0300-9246

DT Journal  
LA English

AB [VO(O2)]+, [HVO2(O2)2]2-, [H2VO2(O2)2]-, [VO(O2)3]3-, [HVO(O2)3]2-, [V(O2)4]3-, [H[V(O2)2]2O]3-, and [VO(NH3)(O2)2]- were identified in aqueous solution on adding H2O2 to [H2VO4]- by 51V NMR spectroscopy. [HVO3(O2)2]2-, [VO2(O2)2]3-, [H2VO3(O2)]-, and [V(OH2)(O2)2]2O were also detected. The chemical shifts and pKa values indicate that the O22- ligands bind to V less covalently than the O ligands, provided that  $\geq 1$  O ligand remains coordinated.

OSC.G 32 THERE ARE 32 CAPLUS RECORDS THAT CITE THIS RECORD (32 CITINGS)

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1958:29055 CAPLUS

DN 52:29055

OREF 52:5189i,5190a

TI Separation of zirconium and hafnium using anion-exchange resins. II. Influence of physical factors

AU Rajan, K. S.; Gupta, J.

CS Natl. Chem. Lab., Poona

SO Journal of Scientific & Industrial Research (1957), 16B, 459-63

CODEN: JSIRAC; ISSN: 0022-4456

DT Journal  
LA Unavailable

AB cf. C.A. 50, 5439c. The influence of the concentration of the eluting H2SO4, the

particle size of the resins, the mode of regeneration of the resin bed, the mode of impregnation of the fluorocomplex, the presence of free fluorides, and the size of the load on the separation of Hf from Zr by anion exchange was studied. Beds of Amberlite IRA-400 or Dowex 2 and 200-mg. samples of K2Zr(Hf)F6 were used. The results were confirmed by successful separation of 5-g. loads of mixed oxides yielding more than 90% Hf-free ZrO2 and 75% spectroscopically pure HfO2.

L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1958:29054 CAPLUS

DN 52:29054

OREF 52:5189g-i

TI Pervanadates in solution  
 AU Souchay, Pierre; Chauveau, Françoise  
 SO Compt. rend. (1957), 245, 1434-6  
 DT Journal  
 LA Unavailable  
 AB The oxidation of vanadates in H<sub>2</sub>O solution shows the different kinds of pervanadates rapidly. Spectrophotometric or cryoscopic examination of the action of H<sub>2</sub>O<sub>2</sub> on metavanadate in Na<sub>2</sub>SO<sub>4</sub> solution shows the presence of Na(VO<sub>3</sub>O<sub>2</sub>) only. In acid solution the preceding ion is converted to a garnet cation (C.A. 36, 40455), (VO<sub>3</sub>O<sub>2</sub>)<sup>-</sup> + 2H<sup>+</sup> → .dblarw. (VO<sub>2</sub>O)<sup>+</sup> + H<sub>2</sub>O<sub>2</sub>. Cryoscopy of the pyrovanadates in the eutectic KNO<sub>3</sub>-H<sub>2</sub>O solution shows evidence of 2 series: K<sub>2</sub>(VO<sub>4</sub>H<sub>2</sub>O<sub>2</sub>) and K<sub>2</sub>(VO<sub>4</sub>H<sub>2</sub>O<sub>3</sub>). The presence of acid pyrovanadates of the type Na<sub>3</sub>HV<sub>2</sub>O<sub>7</sub> are shown in small concns. in vanadic solns., whereas the acid perpyrovanadates such as Na<sub>3</sub>(V<sub>2</sub>O<sub>7</sub>H<sub>2</sub>O<sub>4</sub>) appear clearly in permeta-perpyro mixts. Potentiometric titration curves show the ion corresponding to the salt K<sub>8</sub>V<sub>5</sub>O<sub>26</sub>.2H<sub>2</sub>O. Orthovanadate solns. rich in H<sub>2</sub>O<sub>2</sub> and alkaline base contain blue perorthovanadates of the type Na<sub>3</sub>VO<sub>4</sub>O<sub>4</sub>, which are destroyed by acidification or alkalization.

=> s inositol phosphatases  
     44891 INOSITOL  
     30037 PHOSPHATASES  
 L5 47 INOSITOL PHOSPHATASES  
     (INOSITOL(W)PHOSPHATASES)

=> s 15 and inhibition  
     893756 INHIBITION  
 L6 12 L5 AND INHIBITION

=> d 1-12 bib abs

L6 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2006:1143259 CAPLUS  
 DN 146:24275  
 TI Phosphoinositide-specific inositol polyphosphate 5-phosphatase IV inhibits inositide trisphosphate accumulation in hypothalamus and regulates food intake and body weight  
 AU Bertelli, Daniela F.; Araujo, Eliana P.; Cesquini, Maristela; Stoppa, Graziela R.; Gasparotto-Contessotto, Miriam; Toyama, Marcos H.; Felix, Jorge V. C.; Carvalheira, Jose B.; Michelini, Lisete C.; Chiavegatto, Silvana; Boscherio, Antonio C.; Saad, Mario J. A.; Lopes-Cendes, Iscia; Velloso, Licio A.  
 CS Department of Internal Medicine, State University of Campinas, Campinas, 13083-970, Brazil  
 SO Endocrinology (2006), 147(11), 5385-5399  
 CODEN: ENDOAO; ISSN: 0013-7227  
 PB Endocrine Society  
 DT Journal  
 LA English  
 AB The enzyme phosphatidylinositol 3-kinase (PI3-kinase) exerts an important role in the transduction of the anorexigenic and thermogenic signals delivered by insulin and leptin to first-order neurons of the arcuate nucleus in the hypothalamus. The termination of the intracellular signals generated by the activation of PI3-kinase depends on the coordinated activity of specific inositol phosphatases. Here we show that phosphoinositide-specific inositol polyphosphate 5-phosphatase IV (5ptase IV) is highly expressed in neurons of the arcuate and lateral nuclei of the hypothalamus. Upon intracerebroventricular (ICV) treatment with insulin, 5ptase IV undergoes a time-dependent tyrosine phosphorylation, which follows the same patterns of canonical insulin signaling through the insulin receptor, insulin receptor substrate-2, and

PI3-kinase. To evaluate the participation of 5ptase IV in insulin action in hypothalamus, we used a phosphorothioate-modified antisense oligonucleotide specific for this enzyme. The treatment of rats with this oligonucleotide for 4 d reduced the hypothalamic expression of 5ptase IV by approx. 80%. This was accompanied by an approx. 70% reduction of insulin-induced tyrosine phosphorylation of 5ptase IV and an increase in basal accumulation of phosphorylated inositols in the hypothalamus. Finally, inhibition of hypothalamic 5ptase IV expression by the antisense approach resulted in reduced daily food intake and body weight loss. Thus, 5ptase IV is a powerful regulator of signaling through PI3-kinase in hypothalamus and may become an interesting target for therapeutics of obesity and related disorders.

OSC.G 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (10 CITINGS)  
 RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2009 ACS ON STN  
 AN 2005:1055851 CAPLUS  
 DN 144:34031

TI The amino-terminal non-catalytic region of *Salmonella typhimurium* SigD affects actin organization in yeast and mammalian cells  
 AU Aleman, Ainel; Rodriguez-Escudero, Isabel; Mallo, Gustavo V.; Cid, Victor J.; Molina, Maria; Rotger, Rafael  
 CS Departamento de Microbiología II, Facultad de Farmacia, Universidad Complutense de Madrid, Madrid, 28040, Spain  
 SO Cellular Microbiology (2005), 7(10), 1432-1446  
 CODEN: CEMIF5; ISSN: 1462-5814  
 PB Blackwell Publishing Ltd.  
 DT Journal  
 LA English

AB The internalization of *Salmonella* into epithelial cells relies on the function of bacterial proteins which are injected into the cell by a specialized type III secretion system. Such bacterial effectors interfere with host cell signaling and induce local cytoskeletal rearrangements. One of such effectors is SigD/SopB, which shares homol. with mammalian inositol phosphatases. We made use of the *Saccharomyces cerevisiae* model for elucidating new aspects of SigD function. Endogenous expression of SigD in yeast caused severe growth inhibition. Surprisingly, sigD alleles mutated in the catalytic site or even deleted for the whole C-terminal phosphatase domain still inhibited yeast growth by inducing loss of actin polarization and precluding the budding process. Accordingly, when expressed in HeLa cells, the same sigD alleles lost the ability of depleting phosphatidylinositol 4,5-bisphosphate from the plasma membrane, but still caused disappearance of actin fibers and loss of adherence. We delineate a region of 25 amino acids (residues 118-142) that is necessary for the effect of SigD on actin in HeLa cells. Our data indicate that SigD exerts a toxic effect linked to its N-terminal region and independent of its phosphatase activity.

OSC.G 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (5 CITINGS)  
 RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2009 ACS ON STN  
 AN 2004:1131109 CAPLUS  
 DN 142:193204

TI SHIP Family Inositol Phosphatases Interact with and Negatively Regulate the Tec Tyrosine Kinase  
 AU Tomlinson, Michael G.; Heath, Victoria L.; Turck, Chris W.; Watson, Steve P.; Weiss, Arthur  
 CS Department of Medicine and Howard Hughes Medical Institute, University of California, San Francisco, CA, 94143, USA  
 SO Journal of Biological Chemistry (2004), 279(53), 55089-55096

CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology  
DT Journal  
LA English

AB The Tec family of protein-tyrosine kinases (PTKs), that includes Tec, Itk, Btk, Bmx, and Tkk, plays an essential role in phospholipase C $\gamma$  (PLC $\gamma$ ) activation following antigen receptor stimulation. This function requires activation of phosphatidylinositol 3-kinase (PI 3-kinase), which promotes Tec membrane localization through phosphatidylinositol 3,4,5-trisphosphate (PtdIns 3,4,5-P<sub>3</sub>) generation. The mechanism of neg. regulation of Tec family PTKs is poorly understood. In this study, we show that the inositol 5'-phosphatases SHIP1 and SHIP2 interact preferentially with Tec, compared with other Tec family members. Four lines of evidence suggest that SHIP phosphatases are neg. regulators of Tec. First, SHIP1 and SHIP2 are potent inhibitors of Tec activity. Second, inactivation of the Tec SH3 domain, which is necessary and sufficient for SHIP binding, generates a hyperactive form of Tec. Third, SHIP1 inhibits Tec membrane localization. Finally, constitutively targeting Tec to the membrane relieves SHIP1-mediated inhibition. These data suggest that SHIP phosphatases can interact with and functionally inactivate Tec by dephosphorylation of local PtdIns 3,4,5-P<sub>3</sub> and inhibition of Tec membrane localization.

OSC.G 22 THERE ARE 22 CAPLUS RECORDS THAT CITE THIS RECORD (22 CITINGS)

RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN  
AN 2004:1047762 CAPLUS  
DN 142:73114

TI Two Distinct Tyrosine-based Motifs Enable the Inhibitory Receptor Fc $\gamma$ RIIB to Cooperatively Recruit the Inositol Phosphatases SHIP1/2 and the Adapters Grb2/Gap

AU Isnardi, Isabelle.; Lesourne, Renaud; Bruhns, Pierre; Fridman, Wolf H.; Cambier, John C.; Daeron, Marc

CS Laboratoire d'Immunologie Cellulaire et Clinique, INSERM U255, Institut de Recherches Biomedicales des Cordeliers, Paris, 75006, Fr.

SO Journal of Biological Chemistry (2004), 279(50), 51931-51938  
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology  
DT Journal  
LA English

AB Fc $\gamma$ RIIB are low-affinity receptors for IgG that contain an immunoreceptor tyrosine-based inhibition motif (ITIM) and inhibit immunoreceptor tyrosine-based activation motif (ITAM)-dependent cell activation. When coaggregated with ITAM-bearing receptors, Fc $\gamma$ RIIB become tyrosyl-phosphorylated and recruit the Src homol. 2 (SH2) domain-containing inositol 5'-phosphatases SHIP1 and SHIP2, which mediate inhibition. The Fc $\gamma$ RIIB ITIM was proposed to be necessary and sufficient for recruiting SHIP1/2. We show here that a second tyrosine-containing motif in the intracytoplasmic domain of Fc $\gamma$ RIIB is required for SHIP1/2 to be copptd. with the receptor. This motif functions as a docking site for the SH2 domain-containing adapters Grb2 and Gap. These adapters interact via their C-terminal SH3 domain with SHIP1/2 to form a stable receptor-phosphatase-adaptor trimol. complex. Both Grb2 and Gap are required for an optimal copptn. of SHIP with Fc $\gamma$ RIIB, but one adapter is sufficient for the phosphatase to coppt. in a detectable manner with the receptors. In addition to facilitating the recruitment of SHIPs, the second tyrosine-based motif may confer upon Fc $\gamma$ RIIB the properties of scaffold proteins capable of altering the composition and stability of the signaling complexes generated following receptor engagement.

OSC.G 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)



RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN  
AN 2003:982769 CAPLUS  
DN 140:228218  
TI SHIP2: An emerging target for the treatment of type 2 diabetes mellitus  
AU Baumgartener, James W.  
CS Bainbridge Island, WA, 98110, USA  
SO Current Drug Targets: Immune, Endocrine and Metabolic Disorders (2003),  
3(4), 291-298  
CODEN: CDTIBT; ISSN: 1568-0088  
PB Bentham Science Publishers Ltd.  
DT Journal; General Review  
LA English  
AB A review. With the rapid increase in the number of patients developing type 2 diabetes mellitus and the lack of optimal therapies, much focus has been placed on the insulin-signaling pathway in the discovery of novel drug targets. Phosphatidyl Inositol 3-Kinase (PI3K) is central to mediating insulin's metabolic effects. PI3K catalyzes the generation of phosphatidyl inositol (3,4,5) triphosphate (PIP3). Inhibition of PI3K activity results in a blockade of insulin signaling including glucose uptake and glycogen synthesis. Thus, PIP3 is a critical mediator of insulin action. A family of phosphatidyl inositol phosphatases have been identified that counter-regulate PI3K activity by hydrolyzing PIP3 to phosphatidyl inositol bisphosphate at either the 3' or 5' position of the inositol ring. Mice lacking one of these enzymes, Src-Homol. Inositol Phosphatase-2 (SHIP2), demonstrate increased insulin sensitivity, suggesting that pharmacol. inhibition of SHIP2 could alleviate insulin resistance. Recent studies demonstrate elevated SHIP2 expression is associated with insulin resistance in human patients. Comparing the studies on SHIP2 and other phosphatases suggests how inhibition of SHIP2 leads to increased insulin sensitivity without deleterious effects. This review focuses on the emergence of SHIP2 as a target in the insulin-signaling pathway for the treatment of type 2 diabetes.

OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)  
RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN  
AN 2000:392777 CAPLUS  
DN 133:173793  
TI Cloning and characterization of the mammalian brain-specific, Mg2+-dependent neutral sphingomyelinase  
AU Hofmann, Kay; Tomiuk, Stefan; Wolff, Gabriela; Stoffel, Wilhelm  
CS Bioinformatics and Gene Discovery Group, MEMOREC Stoffel GmbH, Cologne, D-50829, Germany  
SO Proceedings of the National Academy of Sciences of the United States of America (2000), 97(11), 5895-5900  
CODEN: PNASA6; ISSN: 0027-8424  
PB National Academy of Sciences  
DT Journal  
LA English  
AB The enzymic breakdown of sphingomyelin by sphingomyelinases is considered the major source of the second messenger ceramide. Studies on the contribution of the various described acidic and neutral sphingomyelinases to the signaling pool of ceramide have been hampered by the lack of mol. data on the neutral sphingomyelinases (nSMases). We recently identified a mammalian nSMase, an integral membrane protein with remote similarity to bacterial sphingomyelinases. However, its ubiquitous expression pattern is in contrast to previous findings that sphingomyelinase activity is

found mainly in brain tissues. By using an improved database search method, combined with phylogenetic anal., we identified a second mammalian nMase (nMase2) with predominant expression in the brain. The sphingomyelinase activity of nMase2 has a neutral pH optimum, depends on Mg<sup>2+</sup> ions, and is activated by unsatd. fatty acids and phosphatidylserine. Immunofluorescence reveals a neuron-specific punctate perinuclear staining, which colocalizes with a Golgi marker in a number of cell lines. The likely identity of nMase2 with ccal, a rat protein involved in contact inhibition of 3Y1 fibroblasts, suggests a role for this enzyme in cell cycle arrest. Both mammalian nSMases are members of a superfamily of Mg<sup>2+</sup>-dependent phosphohydrolases, which also contains nucleases, inositol phosphatases, and bacterial toxins.

OSC.G 125 THERE ARE 125 CAPLUS RECORDS THAT CITE THIS RECORD (125 CITINGS)  
 RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1998:164967 CAPLUS

DN 128:303899

OREF 128:60073a,60076a

TI Chronic treatment with lithium and pretreatment with excess inositol reduce inositol pool size in astrocytes by different mechanisms

AU Wolfson, Marina; Hertz, Elna; Belmaker, R. H.; Hertz, Leif

CS Faculty of Health Sciences, Department of Microbiology and Immunology and Mental Health Center, Ben Gurion University of the Negev, Beer Sheva, 84105, Israel

SO Brain Research (1998), 787(1), 34-40

CODEN: BRREAP; ISSN: 0006-8993

PB Elsevier Science B.V.

DT Journal

LA English

AB Chronic treatment with a lithium salt is the classical treatment for manic-depressive disorder. It is hypothesized that the therapeutic action of lithium is caused by its inhibition of inositol phosphatases which leads to a relative deficiency of inositol and, therefore, an impairment of inositol recycling and production of precursor for the second messengers inositol triphosphate (IP<sub>3</sub>) and diacylglycerol (DAG). However, peculiarly enough, treatment with high doses of inositol also has an antidepressant effect. In the present work, we have studied the acute and chronic effects of lithium and of excess inositol, in separation or together, on accumulation of 50  $\mu$ M [<sup>3</sup>H]inositol (a physiologically relevant concentration) into primary cultures of mouse astrocytes. Two parameters were investigated: (1) rate of unidirectional uptake across the cell membrane (measured during short-term exposure to the radioisotope), and (2) magnitude of the intracellular pool of inositol, equilibrating with extracellular inositol (measured during long-term exposure to the radioisotope). Inositol uptake was highly concentrative and occurred with a K<sub>m</sub> of approx. 500  $\mu$ M and a V<sub>max</sub> of 1.5 nmol/min/mg protein. The uptake rate was not affected by either acute or chronic treatment with LiCl (or both), but it was substantially reduced ('down-regulated') after pretreatment with a high concentration of inositol. The inositol pool size was decreased to a similar extent as the uptake rate by previous exposure to excess inositol. In spite of the fact that inositol uptake rate was unaffected by lithium, the magnitude of the inositol pool was significantly decreased by chronic treatment with a pharmacologically relevant concentration of LiCl (1 mM), but not by treatment with lower concentrations. This decrease is likely to reflect a reduction in either inositol synthesis or replenishment of inositol from IP<sub>3</sub>, due to the inhibition of inositol phosphatases by the lithium ion. In agreement with the different mechanisms by which lithium and pretreatment with excess inositol appear to reduce the pool size of inositol, the effects of

pretreatment with excess inositol and of LiCl were additive. It is noteworthy that both effects could be observed in astrocytes, suggesting that there might be a significant astrocytic target during clin. treatment.

OSC.G 16 THERE ARE 16 CAPLUS RECORDS THAT CITE THIS RECORD (16 CITINGS)

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2009 ACS ON STN

AN 1997:433964 CAPLUS

DN 127:174957

OREF 127:33889a,33892a

TI Inhibitory receptors, ITIM sequences and phosphatases

AU Unkeless, Jay C.; Jin, Jie

CS Dep. of Biochemistry, Mount Sinai School of Medicine, New York City, NY, 10029, USA

SO Current Opinion in Immunology (1997), 9(3), 338-343

CODEN: COPIEL; ISSN: 0952-7915

PB Current Biology

DT Journal; General Review

LA English

AB A review with 42 refs. A diverse group of inhibitory receptors, including FcγRII, killer cell inhibitory receptors, and B22, shares an immunoreceptor tyrosine-based inhibition motif (ITIM). Recent studies have shown that this motif, when phosphorylated on tyrosine, forms a docking site for the Src homol. 2 recognition domains of the protein tyrosine phosphatase SHP-1 and the inositol 5-phosphatase SHIP. A similar motif in cytotoxic T-lymphocyte antigen-4 recruits the related tyrosine phosphatase SHP-2. These three enzymes act to inhibit signaling cascades resulting from ligation of the BCR, TCR, FcγRIII, and FcεRI, although the relative importance of the tyrosine phosphatases and the inositol phosphatases differs depending on the cell type.

OSC.G 96 THERE ARE 96 CAPLUS RECORDS THAT CITE THIS RECORD (97 CITINGS)

L6 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2009 ACS ON STN

AN 1993:183289 CAPLUS

DN 118:183289

OREF 118:31191a,31194a

TI Lithium chloride depresses calcium-activated force and noradrenaline-induced tension transients in α-toxin permeabilized rat anococcygeus

AU Crichton, C. A.; Smith, G. L.

CS Inst. Physiol., Univ. Glasgow, Glasgow, G12 8QQ, UK

SO Lithium (1993), 4(1), 69-75

CODEN: LITHER; ISSN: 0954-1381

DT Journal

LA English

AB Lithium chloride (LiCl), at millimolar levels, depresses agonist-induced responses in a variety of cell types including smooth muscle. It is thought that LiCl has its effect by inhibiting inositol phosphatases. However, recent work suggests that agonist-induced contractions of smooth muscle are depressed by LiCl via a direct effect on the contractile proteins. In this study, a relatively new permeabilization technique using α-toxin from Staphylococcus aureus was used to study the sep. effects of LiCl on (i) Ca<sup>2+</sup>-activated force at a range of steady state [Ca<sup>2+</sup>] (in 10 mM sep. effects of LiCl on (i) Ca<sup>2+</sup>-activated force at a range of steady state [Ca<sup>2+</sup>] (in 10 mM EGTA) and (ii) force production as a result of agonist-induced Ca<sup>2+</sup> release from the sarcoplasmic reticulum (SR) (in 0.2 mM EGTA). The results suggest that LiCl (10 mM) depresses maximum Ca<sup>2+</sup>-activated force ([Ca<sup>2+</sup>] 100 μM) to 71.8%, but has only a small effect on Ca<sup>2+</sup>-sensitivity of tension production by the contractile proteins. Maximal concns. of caffeine were used to

release  $\text{Ca}^{2+}$  from the SR.  $\text{LiCl}$  depressed the caffeine-induced tension transients by an amount predicted by the effect that  $\text{LiCl}$  has directly on the contractile proteins. This suggests that  $\text{LiCl}$  does not affect the caffeine accessible  $\text{Ca}^{2+}$  content of the SR. However, the noradrenaline-induced tension transients were depressed by more than twice the amount predicted by the direct effect of  $\text{LiCl}$  on  $\text{Ca}^{2+}$ -activated force. This suggests that noradrenaline's ability to release  $\text{Ca}^{2+}$  from the SR is impaired by  $\text{LiCl}$ . One possible mechanism for this result is a reduced production of  $\text{Ins}(1,4,5)\text{P}_3$  through the inhibition of inositol phosphatase activity by  $\text{LiCl}$ .

L6 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1991:532609 CAPLUS

DN 115:132609

OREF 115:22653a,22656a

TI A salt-activated inositol 1,3,4,5-tetrakisphosphate 3-phosphatase at the inner surface of the human erythrocyte membrane

AU Estrada-Garcia, Teresa; Craxton, Andrew; Kirk, Christopher J.; Michell, Robert H.

CS Sch. Biochem., Univ. Birmingham, Birmingham, B15 2TT, UK

SO Proceedings of the Royal Society of London, Series B: Biological Sciences (1991), 244(1309), 63-8

CODEN: PRLBA4; ISSN: 0080-4649

DT Journal

LA English

AB The localization of the human erythrocyte membrane  $\text{Ins}(1,3,4,5)\text{P}_4$  3-phosphatase (where  $\text{Ins}$  = inositol and  $\text{P}_4$  = tetrakisphosphate) was investigated by saponin permeabilization of resealed isoionic erythrocyte ghosts. This enzyme is active at the inner face of the plasma membrane, at the same site as a specific 5-phosphatase that degrades both  $\text{Ins}(1,4,5)\text{P}_3$  (where  $\text{P}_3$  = trisphosphate) and  $\text{Ins}(1,3,4,5)\text{P}_4$ . In the presence of EDTA,  $\text{Ins}(1,4,5)\text{P}_3$  was the only product of  $\text{Ins}(1,3,4,5)\text{P}_4$  metabolism. However, when  $\text{Mg}^{2+}$  was present both the 5-phosphatase and the 3-phosphatase attacked  $\text{Ins}(1,3,4,5)\text{P}_4$ , directly forming  $\text{Ins}(1,3,4)\text{P}_3$  and  $\text{Ins}(1,4,5)\text{P}_3$ ; some  $\text{Ins}(1,4,5)\text{P}_2$  (where  $\text{P}_2$  = bisphosphate) was also formed as a product of 5-phosphatase attack on the liberated  $\text{Ins}(1,4,5)\text{P}_3$ . The  $\text{Ins}(1,3,4,5)\text{P}_4$  3-phosphatase was potentially activated by  $\text{KCl}$ , thus making the route of metabolism of  $\text{Ins}(1,3,4,5)\text{P}_4$  by erythrocyte ghosts strikingly sensitive to variations in ionic strength: at cytosolic  $\text{K}^+$  and  $\text{Mg}^{2+}$  levels, 3-phosphatase activity slightly predominated over 5-phosphatase.  $\text{Ins}(1,3,4,5)\text{P}_4$  3-phosphatase was potentially inhibited by  $\text{Ins}-(1,3,4,5,6)\text{P}_5$  and  $\text{InsP}_6$  (where  $\text{P}_5$  and  $\text{P}_6$  are pentakis- and hexakisphosphate, resp.) at levels lower than those often observed within cells. This leaves open the question as to whether the cellular function of inositol polyphosphate 3-phosphatase is to participate in a physiological cycle that interconverts  $\text{Ins}(1,3,4,5)\text{P}_4$  and  $\text{Ins}(1,4,5)\text{P}_3$  or to metabolize other inositol polyphosphates in the cytosol compartment of cells.

OSC.G 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L6 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1991:530502 CAPLUS

DN 115:130502

OREF 115:22253a,22256a

TI Synthetic inositol 1,3,4,5-tetrakisphosphate analogs

AU Hirata, Masato; Kimura, Yuichi; Ishimatsu, Toyohiro; Yanaga, Fumi; Shuto, Toshihide; Sasaguri, Toshiyuki; Koga, Toshitaka; Watanabe, Yutaka; Ozaki, Shoichiro

CS Fac. Dent., Kyushu Univ., Fukuoka, 812, Japan

SO Biochemical Journal (1991), 276(2), 333-6

CODEN: BIJOAK; ISSN: 0306-3275

DT Journal

LA English

AB Inositol 1,3,4,5-tetrakisphosphate [Ins(1,3,4,5)P4] analogs were synthesized and their effects on [3H]Ins(1,3,4,5)P4 5-phosphatase, [3H]Ins(1,3,4,5)P4 3-phosphatase, and [3H]inositol 1,4,5-trisphosphate [[3H]Ins(1,4,5)P3] 5-phosphatase activities were examined. The Ins(1,3,4,5)P4 analog with an aminobenzoyl group at the 2-position of Ins(1,3,4,5)P4 inhibited the hydrolysis of the 5-phosphate of [3H]Ins(1,3,4,5)P4 catalyzed by erythrocyte ghosts, with a lower  $K_i$  than seen with Ins(1,3,4,5)P4, whereas the analog with an aminocyclohexanecarbonyl group at the same position had a higher  $K_i$  value. Ins(1,4,5)P3 analogs previously synthesized were also capable of inhibiting this process with the same tendency as Ins(1,3,4,5)P4 analogs. Such differences in the potency among Ins(1,3,4,5)P4 and Ins(1,4,5)P3 analogs were applicable to other phosphatase activities, namely [3H]Ins(1,3,4,5)P4 3-phosphatase and [3H]Ins(1,4,5)P3 5-phosphatase. The results suggested that the active sites of these enzymes may catalyze the dephosphorylation in a similar fashion.

L6 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1988:567020 CAPLUS

DN 109:167020

OREF 109:27627a,27630a

TI Two dephosphorylation pathways of inositol 1,4,5-trisphosphate in homogenates of the cellular slime mold Dictyostelium discoideum

AU Van Lookeren Campagne, Michiel M.; Erneux, Christophe; Van Eijk, Ronald; Van Haastert, Peter J. M.

CS Zool. Lab., Univ. Leiden, Leiden, NL-2311 GP, Neth.

SO Biochemical Journal (1988), 254(2), 343-50

CODEN: BIJOAK; ISSN: 0306-3275

DT Journal

LA English

AB D. discoideum Homogenates contain phosphatase activity which rapidly dephosphorylates Ins(1,4,5)P3 (D-myo-inositol 1,4,5-trisphosphate) to Ins (myo-inositol). When assayed in  $Mg^{2+}$ , Ins(1,4,5)P3 is dephosphorylated by the soluble Dictyostelium cell fraction to 20% Ins(1,4)P2 (D-myo-inositol 1,4-bisphosphate) and 80% Ins(4,5)P2 (D-myo-inositol 4,5-bisphosphate). In the particulate fraction, Ins(1,4,5)P3 5-phosphatase is relatively more active than the Ins(1,4,5)P3 1-phosphatase.  $CaCl_2$  can replace  $MgCl_2$  only for the Ins(1,4,5)P3 5-phosphatase activity. Ins(1,4)P2 and Ins(4,5)P2 are both further dephosphorylated to Ins4P(D-myo-inositol 4-monophosphate), and ultimately to Ins.  $Li^+$  ions inhibit Ins(1,4,5)P3 1-phosphatase, Ins(1,4)P2 1-phosphatase, Ins4P phosphatase and L-Ins1P (L-myo-inositol 1-monophosphate) phosphatase activities; Ins(1,4,5)P3 1-phosphatase is 10-fold more sensitive to  $Li^+$  (half-maximal inhibition at about 0.25 mM) than are the other phosphatases (half-maximal inhibition of about 2.5 mM). Ins(1,4,5)P3 5-phosphatase activity is potentially inhibited by 2,3-bisphosphoglycerate (half-maximal inhibition at 3  $\mu M$ ). Furthermore, 2,3-bisphosphoglycerate also inhibits dephosphorylation of Ins(4,5)P2. These characteristics point to a number of similarities between Dictyostelium phospho-inositol phosphatases and those from higher organisms. The presence of an hitherto undescribed Ins(1,4,5)P3 1-phosphatase, however, causes the formation of a different inositol bisphosphatase isomer [Ins(4,5)P2] from that found in higher organisms [Ins(1,4)P2]. The high sensitivity of some of these phosphatases for  $Li^+$  suggests that they may be the targets for  $Li^+$  during the alteration of cell pattern by  $Li^+$  in Dictyostelium.

OSC.G 7 THERE ARE 7 CAPLUS RECORDS THAT CITE THIS RECORD (7 CITINGS)

=> s 15 and apoptosis

195535 APOPTOSIS

L7 2 L5 AND APOPTOSIS

=> d 1-2 bib abs

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN  
AN 2006:592435 CAPLUS  
DN 145:225578  
TI Characterization of the murine Inpp4b gene and identification of a novel isoform  
AU Ferron, Mathieu; Vacher, Jean  
CS Institut de recherches cliniques de Montreal, Montreal, QC, H2W 1R7, Can.  
SO Gene (2006), 376(1), 152-161  
CODEN: GENED6; ISSN: 0378-1119  
PB Elsevier B.V.  
DT Journal  
LA English  
AB Inositol polyphosphate phosphatases and phosphoinositides second messengers have been associated with major cellular functions as growth, differentiation, apoptosis, protein trafficking, and motility. To characterize the role of inositol phosphatases in cell physiolo., mouse inositol polyphosphate 4-phosphatase type II (Inpp4b) cDNA was isolated. The murine Inpp4b locus was mapped on chromosome 8 in a syntenic region of the human 4q27-31 interval between 11-15 and Usp38. The mouse Inpp4b proteins,  $\alpha$  and  $\beta$  isoforms, encoded by this locus contained 927 and 941 amino acids, resp., with a consensus phosphatase catalytic site and a conserved C2 domain highly similar to the human and rat homologs. A novel shorter isoform of Inpp4b $\alpha$  resulted from an alternative translation initiation site and exon 5 skipping. The Inpp4b C2 domain interacted with preferential affinity to phosphatidic acid and phosphatidylinositol 3,4,5-trisphosphate (PI(3,4,5)P3) lipids. Although anal. of Inpp4b transcript and protein expression demonstrated a broad tissue distribution for the  $\alpha$  isoform, as well as for the paralog Inpp4 $\alpha$  and  $\beta$  isoforms, it also displayed a limited hematopoietic lineage distribution whereas the Inpp4b $\beta$  isoform had a highly restricted pattern. Importantly, the Inpp4b $\beta$  localized to the Golgi apparatus whereas Inpp4b $\alpha$  was mainly cytosolic, suggesting a different cellular function for this isoform. This characterization of the murine Inpp4b gene expression pattern, cellular sublocalization, and interacting lipids support a highly specific function for individual Inpp4 phosphatase proteins.  
OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)  
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN  
AN 2005:523467 CAPLUS  
DN 143:53531  
TI Vanadium compounds as inhibitors of phosphatases  
IN Woscholski, Rudiger; Rosivatz, Erika; Vilar, Ramon  
SO Imperial College Innovations Limited, UK  
PA PCT Int. Appl., 58 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005054257	A1	20050616	WO 2004-GB5080	20041206
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,			

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,  
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
 MR, NE, SN, TD, TG

AU 2004295169	A1	20050616	AU 2004-295169	20041206
CA 2547759	A1	20050616	CA 2004-2547759	20041206
EP 1694688	A1	20060830	EP 2004-805909	20041206

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS

CN 1914215	A	20070214	CN 2004-80041315	20041206
JP 2007515406	T	20070614	JP 2006-542013	20041206
IN 2006DN03122	A	20070824	IN 2006-DN3122	20060531
US 20070292532	A1	20071220	US 2007-581000	20070510

PRAI GB 2003-28157 A 20031204  
 WO 2004-GB5080 W 20041206

# ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

OS MARPAT 143:53531

AB Novel Vanadium compds. are described as well as their use as inhibitors of  
 phosphatases, particularly inositol phosphatases. The  
 use of the compound in the treatment of neurodegenerative diseases is also  
 described.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 15 and oxovanadate  
 167 OXOVANADATE  
 L8 0 L5 AND OXOVANADATE

=> oxovanadate and bisperoxo  
 OXOVANADATE IS NOT A RECOGNIZED COMMAND  
 The previous command name entered was not recognized by the system.  
 For a list of commands available to you in the current file, enter  
 "HELP COMMANDS" at an arrow prompt (=>).

=> s oxovanadate and bisperoxo  
 167 OXOVANADATE  
 47 BISPEROXO  
 L9 28 OXOVANADATE AND BISPEROXO

=> s 19 and phosphatases  
 30037 PHOSPHATASES  
 L10 9 L9 AND PHOSPHATASES

=> d 1-9 bib abs

L10 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2008:1149439 CAPLUS  
 DN 149:347863  
 TI Compartmentalization and in vivo insulin-induced translocation of the  
 insulin-signaling inhibitor Grb14 in rat liver  
 AU Desbuquois, Bernard; Bereziat, Veronique; Authier, Francois; Girard, Jean;  
 Burnol, Anne-Francoise  
 CS Institut Cochin, CNRS (UMR 8104), Universite Paris Descartes, Fr.  
 SO FEBS Journal (2008), 275(17), 4363-4377  
 CODEN: FJEOAC; ISSN: 1742-464X  
 PB Wiley-Blackwell  
 DT Journal  
 LA English  
 AB The mol. adaptor Grb14 binds in vitro to the activated insulin receptor

(IR) and inhibits IR signaling. In this study, we have used rat liver subcellular fractionation to analyze in vivo insulin effects on Grb14 compartmentalization and IR phosphorylation and activity. In control rats, Grb14 was recovered mainly in microsomal and cytosolic fractions, but was also detectable at low levels in plasma membrane and Golgi/endosome fractions. Insulin injection led to a rapid and dose-dependent increase in Grb14 content, first in the plasma membrane fraction, and then in the Golgi/endosome fraction, which paralleled the increase in IR  $\beta$ -subunit tyrosine phosphorylation. Upon sustained in vivo IR tyrosine phosphorylation induced by high-affinity insulin analogs, in vitro IR dephosphorylation by endogenous phosphatases, and in vivo phosphorylation of the IR induced by injection of bisperoxo (1,10-phenanthroline)oxovanadate, a phosphotyrosine phosphatase inhibitor, we observed a striking correlation between IR phosphorylation state and Grb14 content in both the plasma membrane and Golgi/endosome fractions. In addition, coimmunoprecipitation experiments provided evidence that Grb14 was associated with phosphorylated IR  $\beta$ -subunit in these fractions. Altogether, these data support a model whereby insulin stimulates the recruitment of endogenous Grb14 to the activated IR at the plasma membrane, and induces internalization of the Grb14-IR complex in endosomes. Removal of Grb14 from fractions of insulin-treated rats by KCl treatment led to an increase of in vivo insulin-stimulated IR tyrosine kinase activity, indicating that endogenous Grb14 exerts a negative feedback control on IR catalytic activity. This study thus demonstrates that Grb14 is a physiological regulator of liver insulin signaling.

OSC.G 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)  
 RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2008:891552 CAPLUS

DN 149:299530

TI Small-molecule protein tyrosine phosphatase inhibition as a neuroprotective treatment after spinal cord injury in adult rats

AU Nakashima, Shojiro; Arnold, Sheila A.; Mahoney, Edward T.; Sithu, Srinivas; Zhang, Y. Ping; D'Souza, Stanley E.; Shields, Christopher B.; Hagg, Theo

CS Department of Neurological Surgery, University of Louisville, Louisville, KY, 40292, USA

SO Journal of Neuroscience (2008), 28(29), 7293-7303

CODEN: JNRSDS; ISSN: 0270-6474

PB Society for Neuroscience

DT Journal

LA English

AB Spinal cord injury causes progressive secondary tissue degeneration, leaving many injured people with neurological disabilities. There are no satisfactory neuroprotective treatments. Protein tyrosine phosphatases inactivate neurotrophic factor receptors and downstream intracellular signaling molecules. Thus, we tested whether the peroxovanadium compound potassium bisperoxo(1,10-phenanthroline)oxovanadate (V) [bpV(phen)], a stable, potent and selective protein tyrosine phosphatase inhibitor, would be neuroprotective after a thoracic spinal cord contusion in adult rats. Intrathecal bpV(phen) infusions through a lumbar puncture rescued dorsal column sensory axons innervating the nucleus gracilis and white matter at the injury epicenter. At the most ED, essentially all of these axons and most of the white matter at the epicenter were spared (vs. approx. 60% with control infusions). BpV(phen) treatments started 4 h after contusion were fully effective. This treatment greatly improved and normalized sensorimotor function in a grid-walking test and provided complete axonal protection over 6 wk. The treatment rescued sensory-evoked potentials that disappeared after dorsal column transection. BpV(phen) affected early



degenerative mechanisms, because the main effects were seen at 7 d and lasted beyond the treatment period. The neuroprotection appeared to be mediated by rescue of blood vessels. BpV(phen) reduced apoptosis of cultured endothelial cells. These results show that a small mol., used in a clin. relevant manner, reduces loss of long-projecting axons, myelin, blood vessels, and function in a model relevant to the most common type of spinal cord injury in humans. They reveal a novel mechanism of spinal cord degeneration involving protein tyrosine phosphatases that can be targeted with therapeutic drugs.

L10 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2007:1088430 CAPLUS

DN 147:462623

TI The control of phosphatidylinositol 3,4-bisphosphate concentrations by activation of the Src homology 2 domain containing inositol polyphosphate 5-phosphatase 2, SHIP2

AU Batty, Ian H.; van der kaay, Jeroen; Gray, Alex; Telfer, Joan F.; Dixon, Miles J.; Downes, C. Peter

CS Division of Molecular Physiology, School of Life Sciences, James Black Centre, University of Dundee, Dundee, DD1 5EH, UK

SO Biochemical Journal (2007), 407(2), 255-266

CODEN: BIJOAK; ISSN: 0264-6021

PB Portland Press Ltd.

DT Journal

LA English

AB Activation of class Ia PI3K (phosphoinositide 3-kinase) produces PtdInsP3, a vital intracellular mediator whose degradation generates addnl. lipid signals. In the present study vanadate analogs that inhibit PTPs (protein tyrosine phosphatases) were used to probe the mechanisms which regulate the concns. of these mols. allowing their independent or integrated function. In 1321N1 cells, which lack PtdInsP3 3-phosphatase activity, sodium vanadate or a cell permeable derivative, bpV(phen) [potassium bisperoxo(1,10-phenanthroline)oxovanadate (V)], increased the recruitment into anti-phosphotyrosine immunoppts. of PI3K activity and of the p85 and p110 $\alpha$  subunits of class Ia PI3K and enhanced the recruitment of PI3K activity stimulated by PDGF (platelet-derived growth factor). However, neither inhibitor much increased cellular PtdInsP3 concns., but both diminished dramatically the accumulation of PtdInsP3 stimulated by PDGF or insulin and markedly increased the control and stimulated concns. of PtdIns(3,4)P2. These actions were accounted for by the ability of PTP inhibitors to stimulate the activity of endogenous PtdInsP3 5-phosphatase(s), particularly SHIP2 (Src homol. 2 domain containing inositol polyphosphate 5-phosphatase 2) and to inhibit types I and II PtdIns(3,4)P2 4-phosphatases. Thus bpV(phen) promoted the translocation of SHIP2 from the cytosol to a Triton X-100-insol. fraction and induced a marked (5-10-fold) increase in SHIP2 specific activity mediated by enhanced tyrosine phosphorylation. The net effect of these inhibitors was, therefore, to switch the signal output of class I PI3K from PtdInsP3 to PtdIns(3,4)P2. A key component controlling this shift in the balance of lipid signals is the activation of SHIP2 by increased tyrosine phosphorylation, an effect observed in HeLa cells in response to both PTP inhibitors and epidermal growth factor.

OSC.G 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)

RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2006:98302 CAPLUS

DN 144:267597

TI Insulin receptor kinase-associated phosphotyrosine phosphatases in hepatic endosomes: assessing the role of phosphotyrosine phosphatase-1B

AU Li, Chaoyang; Baquiran, Gerry; Gu, Feng; Tremblay, Michel L.; Fazel, Ali;

Bergeron, John J. M.; Posner, Barry I.  
 CS Polypeptide Hormone Laboratory, McGill Cancer Center, Montreal, QC, H3A  
 2B2, Can.  
 SO Endocrinology (2006), 147(2), 912-918  
 CODEN: ENDOAO; ISSN: 0013-7227  
 PB Endocrine Society  
 DT Journal  
 LA English  
 AB Previous work has shown that bisperoxo(1,10-phenanthroline)-  
 oxovanadate(v) anion [bpV(phen)] induces potent insulin-mimicking  
 effects in the rat, selectively activates the endosomal (EN) insulin  
 receptor kinase (IRK) in liver, and markedly abolishes endosomal  
 IRK-associated phosphotyrosine phosphatase (PTP) activity while reducing that  
 of total ENs by approx. 30%. In this study the authors examined the  
 relatively selective effect of bpv(phen) on endosomal PTP activities for  
 the purpose of defining IRK-associated PTP(s). Using an in-gel PTP assay,  
 the authors detected multiple (.apprx.20) species of endosomal PTP (30 to  
 >220 kDa), with five that were markedly inhibited after in vivo bpV(phen)  
 administration. Using a combination of Mono Q anionic exchange chromatog.  
 and immunoblotting, the authors demonstrated that LAR (leukocyte common  
 antigen-related), PTP- $\alpha$ , and PTP-1B were present in endosomal  
 subfractions not significantly inhibited by bpv(phen). PTP-1B activity  
 was assayed in immunoppts. from hepatic ENs of control and  
 bpV(phen)-treated rats and was found to be inhibited by approx. 30% after  
 bpv(phen) treatment. To clarify the role of PTP-1B in dephosphorylating  
 IRK, the authors prepared hepatic ENs from wild-type and PTP-1B-null mice.  
 The authors found that the phosphotyrosine content of IRK was similar in  
 these two types of ENs, and that IRK dephosphorylation was not affected in  
 ENs from PTP-1B-null mice compared with that in ENs from wild-type mice.  
 These data suggest that LAR, PTP- $\alpha$ , and PTP-1B are not candidates  
 for the IRK-associated PTP in hepatic ENs, and that IRK dephosphorylation in  
 ENs may result from the concerted actions of several PTPs.

OSC.G 1 THERE ARE 1 CAPLUS RECORDS THAT CITE THIS RECORD (1 CITINGS)  
 RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 2005:1034190 CAPLUS  
 DN 143:401589  
 TI Reactive Oxygen Species Induce Tyrosine Phosphorylation of and Src Kinase  
 Recruitment to NO-sensitive Guanylyl Cyclase  
 AU Meurer, Sabine; Pioch, Sylke; Gross, Steffen; Mueller-Esterl, Werner  
 CS Institute for Biochemistry II, University of Frankfurt Medical School,  
 Frankfurt, D-60590, Germany  
 SO Journal of Biological Chemistry (2005), 280(39), 33149-33156  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English  
 AB Soluble guanylyl cyclase (sGC) is the major cytosolic receptor for nitric  
 oxide (NO) that converts GTP into the second messenger cGMP in a  
 NO-dependent manner. Other factors controlling this key enzyme are  
 intracellular proteins such as Hsp90 and PSD95, which bind to sGC and  
 modulate its activity, stability, and localization. To date little is  
 known about the effects of posttranslational modifications of sGC,  
 although circumstantial evidence suggests that reversible phosphorylation  
 may contribute to sGC regulation. Here we demonstrate that inhibitors of  
 protein-tyrosine phosphatases such as pervanadate and  
 bisperoxo(1,10-phenanthroline)oxovanadate(V) as well as  
 reactive oxygen species such as H2O2 induce specific tyrosine  
 phosphorylation of the  $\beta$ 1 but not of the  $\alpha$ 1 subunit of sGC.  
 Tyrosine phosphorylation of sGC $\beta$ 1 is also inducible by pervanadate

and H2O2 in intact PC12 cells, rat aortic smooth muscle cells, and in rat aortic tissues, indicating that tyrosine phosphorylation of sGC may also occur in vivo. We have mapped the major tyrosine phosphorylation site to position 192 of  $\beta 1$ , where it forms part of a highly acidic phospho-acceptor site for Src-like kinases. In the phosphorylated state Tyr(P)-192 exposes a docking site for SH2 domains and efficiently recruits Src and Fyn to sGC $\beta 1$ , thereby promoting multiple phosphorylation of the enzyme. Our results demonstrate that sGC is subject to tyrosine phosphorylation and interaction with Src-like kinases, revealing an unexpected cross-talk between the NO/cGMP and tyrosine kinase signaling pathways at the level of sGC.

OSC.G 21 THERE ARE 21 CAPLUS RECORDS THAT CITE THIS RECORD (21 CITINGS)  
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2005:1017325 CAPLUS

DN 143:322823

TI Constitutive secretion of serum albumin requires reversible protein tyrosine phosphorylation events in trans-Golgi

AU Webb, Rachel J.; Judah, Jacob D.; Lo, Lee-Chiang; Thomas, Geraint M. H.

CS Department of Physiology, University College London, London, UK

SO American Journal of Physiology (2005), 289(3, Pt. 1), C748-C756

CODEN: AJPHAP; ISSN: 0002-9513

PB American Physiological Society

DT Journal

LA English

AB Serum albumin secretion from rat hepatocytes proceeds via the constitutive pathway. Although much is known about the role of protein tyrosine phosphorylation in regulated secretion, nothing is known about its function in the constitutive process. Here we show that albumin secretion is inhibited by the tyrosine kinase inhibitor genistein but relatively insensitive to subtype-selective inhibitors or treatments. Secretion is also blocked in a physiol. identical manner by the tyrosine phosphatase inhibitors pervanadate and bisperoxo(1,10-phenanthroline)-oxovanadate. Inhibition of either the kinase(s) or phosphatase(s) leads to the accumulation of albumin between the trans-Golgi and the plasma membrane, whereas the immediate precursor proalbumin builds up in a proximal compartment. The trans-Golgi marker TGN38 is rapidly dispersed under conditions that inhibit tyrosine phosphatase action, whereas the distribution of the cis-Golgi marker GM130 is insensitive to genistein or pervanadate. By using a specifically reactive biotinylation probe, we detected protein tyrosine phosphatases in highly purified rat liver Golgi membranes. These membranes also contain both endogenous tyrosine kinases and their substrates, indicating that enzymes and substrates for reversible tyrosine phosphorylation are normal membrane-resident components of this trafficking compartment. In the absence of perturbation of actin filaments and microtubules, we conclude that reversible protein tyrosine phosphorylation in the trans-Golgi network is essential for albumin secretion and propose that the constitutive secretion of albumin is in fact a regulated process.

OSC.G 6 THERE ARE 6 CAPLUS RECORDS THAT CITE THIS RECORD (6 CITINGS)  
RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

AN 2001:351257 CAPLUS

DN 135:147697

TI Role of PRL-3, a human muscle-specific tyrosine phosphatase, in angiotensin-II signaling

AU Matter, William F.; Estridge, Thomas; Zhang, Chen; Belagaje, Rama;

Stancato, Louis; Dixon, Jeff; Johnson, Brian; Bloem, Laura; Pickard, Todd;

Donaghue, Mary; Acton, Susan; Jeyaseelan, Raju; Kadambi, Vivek; Vlahos, Chris J.  
 CS Cardiovascular Research, Eli Lilly and Company, Indianapolis, IN, 46285, USA  
 SO Biochemical and Biophysical Research Communications (2001), 283(5), 1061-1068  
 CODEN: BBRCA9; ISSN: 0006-291X  
 PB Academic Press  
 DT Journal  
 LA English  
 AB Action of protein kinases and phosphatases contributes to myocardial hypertrophy. PRL-3, a protein tyrosine phosphatase, was identified in a cDNA library from an explanted human heart obtained from a patient with idiopathic cardiomyopathy. PRL-3 is expressed in heart and skeletal muscle, exhibiting approx. 76% identity to the ubiquitous tyrosine phosphatase PRL-1, which was reported to increase cell proliferation. PRL-3 was cloned into E. coli and purified using affinity chromatog. PRL-3 activity was determined using the substrate 6,8-difluoro-4-methylumbelliferyl phosphate, and was inhibited by vanadate and analogs. HEK293 cells expressing PRL-3 demonstrated increased growth rates vs. nontransfected cells or cells transfected with the catalytically inactive C104S PRL-3 mutant. The tyrosine phosphatase inhibitor, potassium bisperoxo (bipyridine) oxovanadate V, normalizes the growth rate of PRL-3 expressing cells to that of parental HEK293 cells in a concentration-dependent manner. Using FLIPR anal., parental HEK293 cells mobilize calcium when stimulated with angiotensin-II (AngII). However, calcium mobilization is inhibited in cells expressing wild-type PRL-3 when stimulated with AngII, while cells expressing the inactive mutant of PRL-3 mobilize calcium to the same extent as parental HEK293 cells. Western blots comparing PRL-3 transfected cells to parental HEK293 cells showed dephosphorylation of p130cas in response to AngII. These data suggest a role for PRL-3 in the modulation of intracellular calcium transients induced by AngII. (c) 2001 Academic Press.

OSC.G 46 THERE ARE 46 CAPLUS RECORDS THAT CITE THIS RECORD (46 CITINGS)  
 RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN  
 AN 1998:383106 CAPLUS  
 DN 129:117463  
 OREF 129:23925a  
 TI Modulation of interferon- $\gamma$ -induced macrophage activation by phosphotyrosine phosphatases inhibition. Effect on murine leishmaniasis progression

AU Olivier, Martin; Romero-Gallo, Bertha-Judith; Matte, Claudine; Blanchette, Julie; Posner, Barry I.; Tremblay, Michel J.; Faure, Robert  
 CS Centre de Recherche en Infectiologie et Departement de Biologie Medicale, Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, Universite Laval, Ste-Foy, QC, G1V 4G2, Can.

SO Journal of Biological Chemistry (1998), 273(22), 13944-13949  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English  
 AB Phagocyte functions are markedly inhibited after infection with the intracellular protozoan parasite Leishmania. This situation strongly favors the installation and propagation of this pathogen within its mammalian host. Previous findings by us and others have established that alteration of several signaling pathways (protein kinase C-, Ca<sup>2+</sup>- and protein-tyrosine kinases-dependent signaling events) were directly responsible for Leishmania-induced macrophage (MO) dysfunctions. Here we report that modulation of phosphotyrosine-dependent events with a protein

tyrosine phosphatases (PTP) inhibitor, the peroxovanadium (pV) compound bpV(phen) (potassium bisperoxo(1,10-phenanthroline) oxovanadate(VI)), can control host-pathogen interactions by different mechanisms. We observed that the inhibition of parasite PTP resulted in an arrest of proliferation and death of the latter in coincidence with cyclin-dependent kinase (CDK1) tyrosine 15 phosphorylation. Moreover the treatment of MO with bpV(phen) resulted in an increased sensitivity to interferon- $\gamma$  stimulation, which was reflected by enhanced nitric oxide (NO) production. This enhanced IFN- $\gamma$ -induced NO generation was accompanied by a marked increase of inducible nitric oxide synthase (iNOS) mRNA gene and protein expression. Finally we have verified the in vivo potency of bpV(phen) over a 6-wk period of daily administration of a sub-toxic dose. The results revealed its effectiveness in controlling the progression of visceral and cutaneous leishmaniasis. Therefore PTP inhibition of Leishmania and MO by the pV compound bpV(phen) can differentially affect these eukaryotic cells. This strongly suggests that PTP plays an important role in the progression of Leishmania infection and pathogenesis. The apparent potency of pV compds. along with their relatively simple and versatile structure render them attractive pharmacol. agents for the management of parasitic infections.

OSC.G 63 THERE ARE 63 CAPLUS RECORDS THAT CITE THIS RECORD (63 CITINGS)  
 RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2009 ACS on STN

AN 1995:957165 CAPLUS

DN 124:75749

OREF 124:13833a,13836a

TI Arrest at the G2/M transition of the cell cycle by protein-tyrosine phosphatase inhibition: Studies on a neuronal and a glial cell line

AU Faure, Robert; Vincent, Michel; Dufour, Maurice; Shaver, Alan; Posner, Barry I.

CS Centre Recherche Centre Hospitalier, Universite Laval, QC, G1V4G2, Can.

SO Journal of Cellular Biochemistry (1995), 59(3), 389-401

CODEN: JCEBD5; ISSN: 0730-2312

PB Wiley-Liss

DT Journal

LA English

AB The addition of the peroxovanadium (pV) derivs. potassium bisperoxo (1,10-phenanthroline)oxovanadate(v) (bpV[phen]) or potassium bisperoxo(pyridine-2-carboxylato)oxovanadate(v) (bpV[pic]), both of which are potent inhibitors of protein tyrosine phosphatases (PTPs) [Posner et al. (1994): J Biol Chem 269:4596-4604], to the culture medium of neuroblastoma NB 41 and glioma C6 cells resulted in a marked decrease in their proliferation rates and a progressive accumulation at the G2/M transition of the cell cycle. The effect was dependent on dose, cell type, and the pV compound employed. Mean values of the RNA-to-DNA and RNA-to-protein ratios in NB cells treated for 48 h with increased doses of bpV[phen] showed that general synthetic functions were not altered, nor did the authors observe oxidative damage to DNA using a sensitive DNA-nick detection assay. No changes in the expression and localization of vimentin, a component of the intermediate filament cytoskeleton, were observed by indirect immunofluorescence, showing that treatment did not disturb the cytoskeleton network. Measurements of BrdU incorporation into newly synthesized DNA showed that cells treated were not totally arrested. Furthermore, cells arrested at G2/M were able to reenter the cycle rapidly after the release of inhibition. This progressive accumulation at G2/M coincided with the detection of tyrosine-phosphorylated p34cdc2 and a dramatic reduction in its kinase activity toward histone H1 by 48 h of culture. Both compds. were equally potent in inhibiting the catalytic activity of a yeast and the structurally distant mouse cdc25B in vitro, suggesting that the augmented

tyrosine phosphorylation of p34cdc2 derived from the in vivo inhibition of cdc25. Their equal in vitro potency contrasted with the considerably greater potency of bpV[phen] in vivo, suggesting that factors regulating the intracellular access of these compds. to cdc25 might be critical in determining

in vivo specificity. In conclusion the final consequence of long-term exposure to potent and structurally defined PTP inhibitors on two highly proliferative nerve cell lines is to restrict cell growth. The corresponding hyperphosphorylation and reduced activity of p34cdc2 likely reflects the unusual sensitivity of cdc25 as an in vivo target for peroxovanadium compds.

OSC.G 25 THERE ARE 25 CAPLUS RECORDS THAT CITE THIS RECORD (25 CITINGS)

=>

---Logging off of SIN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	122.92	309.02
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-25.42	-25.42
STN INTERNATIONAL LOGOFF AT 18:52:04 ON 19 NOV 2009		